# Geriatric Anesthesia Draft Systematic Review Protocol

## I. Background

Between 2019 and 2060, the number of US adults aged 65 years or older will likely increase from 54 to 95 million; the oldest-old (85+ years) will grow from 6.6 to 19 million over the same period.[1,2] These demographic shifts carry significant implications for the practice of anesthesiology. In 2007, the elderly (15% of the US population) underwent 35% of inpatient surgeries.[3] In 2006, 32% of outpatient surgeries were performed in the elderly.[4] Moreover, the risk of postoperative complications increases with age.[5,6] Improving the quality of perioperative care for older adults is a major priority for patients, providers, and policy makers.

## II. Systematic Review Questions

### *Preoperative care*

1. Among geriatric patients anticipating surgery and anesthesia, does expanded preoperative evaluation (e.g., for frailty, cognitive impairment, functional status, or psychosocial issues) lead to improved postoperative outcomes?
2. Among geriatric patients anticipating surgery and anesthesia, do interventions targeted at improving physical function, cognition, and nutritional status before surgery (“prehabilitation”) improve postoperative outcomes?

### *Intraoperative care*

3. Among geriatric patients undergoing surgery, does regional anesthesia as the primary anesthetic technique improve postoperative outcomes compared with general anesthesia?
4. Among geriatric patients undergoing surgery with general anesthesia, does the use of intravenous agents for maintenance of anesthesia improve postoperative outcomes compared with inhaled agents?
5. Among geriatric patients undergoing surgery and anesthesia, do commonly used potentially inappropriate medications administered during the perioperative period increase the risk of postoperative delirium or other adverse outcomes?
6. Among geriatric patients undergoing surgery and anesthesia, do dexmedetomidine, ketamine, ramelteon, or melatonin administered during the perioperative period decrease the risk of postoperative delirium or other adverse cognitive outcomes?

### *Postoperative care*

7. Among geriatric patients undergoing surgery, do postoperative lower limb regional anesthetic techniques, such as continuous epidural anesthesia improve postoperative outcomes?
8. Does screening geriatric patients for postoperative delirium in the post anesthesia care unit improve postoperative outcomes?

## III. PICOTS

### *Population*

- Patients 65 years or older undergoing general anesthesia, sedation, or regional anesthesia for surgical procedures.
- Subgroups
    - Age
        - 65-74
        - 75-84
        - 85+
    - Sex
    - Race
    - Ethnicity
    - Frailty
    - Mild neurocognitive disorder (mild cognitive impairment)
    - Major neurocognitive disorder (dementia)
    - Elective surgery
    - Emergency surgery
    - Type of procedure
    - ASA classification
        - ASA I-II
        - ASA III or higher

### *Interventions*

*Preoperative*

- Expanded preoperative evaluation (frailty, cognitive, functional, or psychosocial)
    - Primary frailty tools to include (but not limited to)
        - Fried Frailty Index
        - Frailty Index
        - Clinical Frailty Scale
        - Edmonton Frail Scale
        - Risk Analysis Index
- Prehabilitation (functional, cognitive, nutritional)

*Intraoperative*

- Regional anesthesia as the primary anesthetic
- TIVA
- Inhalation agents
- Potentially inappropriate medications
    - Anticholinergics
    - Antipsychotics
    - Corticosteroids
    - Ketorolac and NSAIDs
    - H2-receptor antagonists
    - Benzodiazepines
    - Nonbenzodiazepine benzodiazepine receptor agonist hypnotics: eszopiclone, zaleplon, zolpidem
- Drugs to prevent delirium (dexmedetomidine, ketamine, ramelteon, or melatonin)

*Postoperative*

- Postoperative regional anesthetics for lower limb pain (continuous epidural, nerve block with catheter)
- PACU screening for delirium

### *Comparators*

*Preoperative*

- Standard preoperative evaluation
- No prehabilitation

*Intraoperative*

- Regional anesthesia as the primary anesthetic

- TIVA
- Avoidance of potentially inappropriate medications
- No drugs to prevent delirium

*Postoperative*

- No postoperative regional anesthetics for lower limb pain (continuous epidural, lower limb nerve block with catheter)
- No PACU screening for delirium

Table: Interventions and corresponding comparators.

| | Intervention(s) | Comparator(s) |
|---|---|---|
| *Preoperative* | Expanded preoperative evaluation (frailty, cognitive, functional, psychosocial) | Standard preoperative evaluation |
| | Prehabilitation (functional, cognitive, nutritional) | No prehabilitation |
| *Intraoperative* | Regional anesthesia as the primary anesthetic | General anesthesia |
| | Total intravenous anesthesia | Volatile anesthetics |
| | Anticholinergics<br>Antipsychotics<br>Corticosteroids<br>H2-receptor antagonists<br>Benzodiazepines<br>Nonbenzodiazepine benzodiazepine receptor agonist hypnotics: eszopiclone, zaleplon, zolpidem | None |
| | Drugs to prevent delirium (dexmedetomidine, ketamine, ramelteon, or melatonin) | None |
| *Postoperative* | Postoperative regional anesthetics for lower limb pain (continuous epidural, lower extremity nerve block with catheter) | Opioids, multimodal analgesia not including nerve block, or conventional pain management |
| | Screening for postoperative delirium | No screening for postoperative delirium |

***Outcomes***

- Postoperative delirium
- Delayed neurocognitive recovery (< 30 days after procedure)
- Postoperative neurocognitive disorder (mild, major)
- Major neurocognitive disorder (dementia)
- Mild neurocognitive disorder (mild cognitive impairment)
- Stroke
- Intraoperative awareness
- Recovery (e.g., Aldrete and Quality of Recovery scores)
- Depression
- Patient/caregiver/family satisfaction
- Valued life activities
- Physical functional status (independence/disability)
- Health-related quality of life
- Pain
- Opioid use
- Complications
    - Surgical site infection (superficial, deep)
    - Respiratory (pneumonia, unplanned intubation, pulmonary embolism, on ventilator > 48 hours)
    - Urinary tract infection
    - Acute kidney injury
    - Central nervous system (stroke, nerve injury)

- Cardiac (MI, arrest)
- Deep venous thrombosis
- Sepsis

- Length of stay
- Discharge location
  - Home
  - Rehab/skilled/short-term, long-term care, or other than primary residence
- Readmission
- Mortality

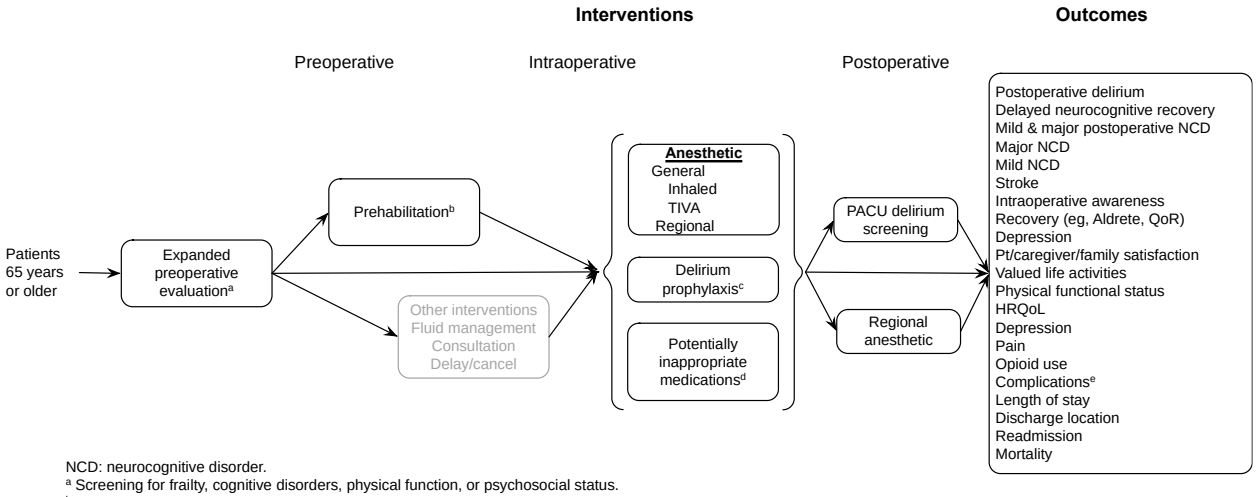
***Timing***

- Perioperative period through 1 year

***Settings***

- Any surgical

## IV. Analytic Framework




NCD: neurocognitive disorder.
[a] Screening for frailty, cognitive disorders, physical function, or psychosocial status.
[b] Functional, cognitive, and nutritional.
[c] Dexmedetomidine, ketamine, remelteon, and melatonin.
[d] Anticholinergics, antipsychotics, corticosteroids, and ketorolac (NSAIDs), H2-receptor antagonists, benzodiazepines, eszopiclone, zaleplon, and zolpidem.
[e] Surgical site infection (superficial, deep), respiratory (pneumonia, unplanned intubation, pulmonary embolism, on ventilator > 48 hours), urinary tract infection, acute kidney injury, central nervous system, cardiac, deep venous thrombosis, and sepsis.

## V. Methods

***Search***

The literature search will include publications from 2000 to present (PubMed, Embase, Scopus, and Cochrane Central).

***Study inclusion/exclusion criteria***

1. Studies of geriatric patients. (Studies including younger patients will be considered if a result is judged transportable to the target population).
2. Publication Types
   - Published journal articles, reports
   - Language restrictions: English language only
   - Limited to humans
   - Grey literature
3. Study Designs
   - Include
     - Randomized clinical trials
     - Non-randomized trials

        - Quasi-randomized designs (e.g., before-after studies, interrupted time series)
        - Cohort studies (prospective, retrospective)
        - Case-control studies
        - Other observational studies (e.g., diagnostic accuracy)
    - Exclude
        - Case reports and case series
        - Surveys, questionnaires
        - Letters
        - Editorials
        - Conference abstracts
        - Systematic reviews and meta-analyses (for reference checking)

***Search Strategies***

(Separate document)

***Data Abstraction and Management***

Title/abstract and full-text screening together with data extraction will be performed on the DistillerSR platform.[7] All screening will be conducted in duplicate, with disagreements resolved by consensus or a third reviewer as needed.

Anticipated data extraction includes study characteristics (e.g., design, dates, setting, centers, country, funding, registration, subgroups, surgery, and anesthetic), study arms (e.g., intervention, participant characteristics, intervention, and outcomes reported), and outcome detail according to type (e.g., patient-reported or clinical; continuous, dichotomous [includes relative effects], rating scales [Likert, visual analog, numeric]). As required, figures will be digitized. A single reviewer will extract study data followed by verification.[8]

***Risk of Bias of Individual Studies***

Risk of bias assessment for randomized trials will be conducted using the Cochrane risk of bias tool. [9] Risk of bias assessment of non-randomized studies of interventions (e.g., observational studies of interventions including cohort, case-control, and quasi-randomized designs) will utilize the Risk Of Bias In Non-randomised Studies of Interventions tool (ROBINS-I).[10] Risk of bias will be assessed independently by two reviewers with discrepancies resolved by discussion, or a third reviewer as needed.

***Evidence Synthesis***

As appropriate, based on clinical and methodological heterogeneity, study results will be pooled in either pairwise or network meta-analyses in random effects models (given the goal of estimating unconditional effects not relevant only to the pooled studies).[11] Statistical heterogeneity is evaluated using between study variance and $I^2$.[12] When there is meaningful heterogeneity and the number of studies sufficient (e.g., 10 or more) meta-regression is considered to explain the variability.[13] With 10 or more pooled studies, small study effects and the potential for publication bias will be examined in funnel plots, regression-based tests, adjustment methods, and p-curves.[14,15]

Relative effects will be pooled as risk ratios for clinical interpretability except when adjusted measures reported as odds are pooled. Continuous measures are pooled as mean differences or standardized mean differences when studies use differing scales. When practicably, standardized mean differences will be re-expressed on the most meaningful scale.[16] R (R Foundation for Statistical Computing, Vienna, Austria) will be used for analyses and data made publicly available when the guideline is completed.

***Grading the Strength of Evidence***

The strength (certainty) of evidence for important outcomes will be appraised using either GRADE[17] and ACCF/AHA[18] frameworks.

***Registration***

TBD

Table. Protocol Development

| Date | Section | Modification |
|---|---|---|
| July 2021 | | First draft |
| June 2022 | Key questions | Key questions removed: EEG monitoring and cognitive function; sedation titration with EEG monitoring; and maintaining intraoperative high blood pressure |

## VI. References


1. Administration on Aging: 2020 Profile of Older Americans, 2021
2. Mather M, Jacobsen L, Kilduff L, Lee A, Pollard K, Scommegna P, Vonorman A: America's Changing Population. Population Bulletin 2019; 74
3. Hall MJ, DeFrances CJ, Williams SN, Golosinskiy A, Schwartzman A: National Hospital Discharge Survey: 2007 summary. Natl Health Stat Report 2010:1-20, 24
4. Cullen KA, Hall MJ, Golosinskiy A: Ambulatory surgery in the United States, 2006. Natl Health Stat Report 2009:1-25
5. Turrentine FE, Wang H, Simpson VB, Jones RS: Surgical risk factors, morbidity, and mortality in elderly patients. J Am Coll Surg 2006; 203:865-77
6. Monk TG, Saini V, Weldon BC, Sigl JC: Anesthetic management and one-year mortality after noncardiac surgery. Anesth Analg 2005; 100:4-10
7. Evidence Partners: DistillerSR. Ottawa, Canada, 2020
8. PCORI: Methodology Standards (11: Standards for Systematic Reviews) https://www.pcori.org/research-results/about-our-research/research-methodology/pcori-methodology-standards#Systematic%20Reviews, 2021
9. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA, Cochrane Bias Methods G, Cochrane Statistical Methods G: The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; 343:d5928
10. Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hrobjartsson A, Kirkham J, Juni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schunemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JP: ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016; 355:i4919
11. Hedges LV, Vevea JL: Fixed-and random-effects models in meta-analysis. Psychological Methods 1998; 3:486
12. Rucker G, Schwarzer G, Carpenter JR, Schumacher M: Undue reliance on I(2) in assessing heterogeneity may mislead. BMC Med Res Methodol 2008; 8:79
13. Thompson SG, Higgins JP: How should meta-regression analyses be undertaken and interpreted? Stat Med 2002; 21:1559-73
14. Schwarzer G, Carpenter JR, Rücker G: Meta-analysis with R, Springer, 2015
15. Simonsohn U, Nelson LD, Simmons JP: p-Curve and Effect Size: Correcting for Publication Bias Using Only Significant Results. Perspect Psychol Sci 2014; 9:666-81
16. Higgins JPT, Cochrane Collaboration: Cochrane handbook for systematic reviews of interventions, Second edition. edition. Hoboken, NJ, Wiley-Blackwell, 2020
17. Schunemann H, Brozek J, Guyatt G, Oxman A: GRADE Handbook, 2019
18. Jacobs AK, Kushner FG, Ettinger SM, Guyton RA, Anderson JL, Ohman EM, Albert NM, Antman EM, Arnett DK, Bertolet M, Bhatt DL, Brindis RG, Creager MA, DeMets DL, Dickersin K, Fonarow GC, Gibbons RJ, Halperin JL, Hochman JS, Koster MA, Normand S-LT, Ortiz E, Peterson ED, Roach JWH, Sacco RL, Smith JSC, Stevenson WG, Tomaselli GF, Yancy CW, Zoghbi WA, Harold JG, He Y, Mangu PB, Qaseem A, Sayre MR, Somerfield MR: ACCF/AHA clinical practice guideline methodology summit report: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013; 61:213-65